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Distal radius fractures — epidemiology and aspects of surgical management

Johanna Rundgren

Karolinska Institutet

DEPARTMENT OF CLINICAL SCIENCE AND EDUCATION,
SÖDERSJUKHUSET
Karolinska Institutet, Stockholm, Sweden

DISTAL RADIUS FRACTURES
– EPIDEMIOLOGY AND ASPECTS OF SURGICAL MANAGEMENT

Johanna Rundgren

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THESIS FOR DOCTORAL DEGREE (Ph.D.)

By

Johanna Rundgren

Principal Supervisor:
Professor Anders Enocson
Karolinska Institutet
Department of Clinical Science and Education, Södersjukhuset *and*
Department of Molecular Medicine and Surgery
Division of Orthopedics

Co-supervisors:
PhD Cecilia Mellstrand Navarro
Karolinska Institutet
Department of Clinical Science and Education, Södersjukhuset
Division of Hand Surgery

Professor Sari Ponzer
Karolinska Institutet
Department of Clinical Science and Education, Södersjukhuset
Division of Orthopedics

Opponent:
Professor Hans Mallmin
Uppsala University
Department of Surgical Sciences
Division of Orthopedics

Examination Board:
Associate professor Emma Larsson
Karolinska Institutet
Department of Physiology and Pharmacology
Division of Anesthesiology

Professor Isam Atroshi
Lund University
Department of Clinical Sciences
Division of Orthopedics

Associate professor Rikard Wedin
Karolinska Institutet
Department of Molecular Medicine and Surgery
Division of Orthopedics

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To my beloved family

ABSTRACT

Distal radius fractures (DRFs) are the most common fractures treated by physicians. About 20% of all DRFs are treated surgically. The main surgical methods are volar plate fixation, external fixation and percutaneous pinning. The spectrum and frequency of associated complications vary considerably between surgical methods. DRF surgery is often performed in a day surgery setting. Anesthesia is achieved by either regional anesthesia (RA) or general anesthesia (GA). An important aspect of treatment outcome evaluation is patient-reported outcome measures (PROMs). The EQ-5D questionnaire is a well-known generic PROM, which measures health-related quality of life (HRQoL). The overall aim of this thesis was to study DRF epidemiology and aspects of surgical management and treatment evaluation.

In *Study I*, the internal and external responsiveness of EQ-5D index score was assessed for 132 patients aged 50-74 years with a surgically treated DRF, whom within the context of a previous randomized controlled trial completed the EQ-5D and the Patient-Rated Wrist Evaluation (PRWE-Swe) questionnaires at baseline (preinjury state), and at 3 and 12 months postoperatively. PRWE-Swe was used as the external criterion. The study showed that EQ-5D index score displayed an overall acceptable to good responsiveness in patients with a surgically treated DRF, and thus may be used as a measure of HRQoL in this patient group.

Study II was a single-center randomized clinical trial comparing RA (with a supraclavicular plexus blockade) and GA in 88 patients aged 18-74 years with a displaced DRF treated with volar plate fixation in day surgery. Outcomes included opioid equivalent consumption (OEC) during the first 3 postoperative days, VAS for pain, perioperative time consumption, and functional outcomes and PROMs at 6 months. The study showed that the anesthesia method significantly influenced the early patterns of postoperative pain and opioid consumption after DRF surgery, as well as the perioperative time consumption. Neither total OEC over the first 3 postoperative days, nor longer-term outcomes differed between the groups.

Study III was a national descriptive cross-sectional register study using data from the Swedish Fracture Register (SFR). Included were 23,394 DRFs in 22,962 patients aged 18 years or older. The study provided comprehensive descriptive data on the epidemiology, classification, injury characteristics, treatment regimens and mortality of DRFs. The most common type of patient was an elderly woman who sustained a DRF through a simple fall at her own residence and whose fracture was extra-articular and treated non-surgically.

Study IV was a nation-wide cohort study linking data from two population-based health-care registers, assessing the rate of surgical site infections after DRF surgery for the three main surgical methods, as well as factors associated with a surgical site infection. A dispensed prescription of Flucloxacillin and/or Clindamycin within eight weeks after DRF surgery was used as a proxy for a surgical site infection. A total of 31,807 patients 18 years or older with a surgically treated DRF were included. The rate of surgical site infection was 28% for external fixation, 12% for percutaneous pinning and 5% for plate fixation.

LIST OF SCIENTIFIC PAPERS

This thesis is based on the following papers, which are referred to in the text by their Roman numerals (Study I-IV):

I. RESPONSIVENESS OF EQ-5D IN PATIENTS WITH A DISTAL RADIUS FRACTURE
Rundgren J, Enocson A, Mellstrand Navarro C, Bergström G.
Hand (N Y). 2018;13(5):572-580.

II. REGIONAL OR GENERAL ANESTHESIA IN THE SURGICAL TREATMENT OF DISTAL RADIAL FRACTURES: A RANDOMIZED CLINICAL TRIAL
Rundgren J, Mellstrand Navarro C, Ponzer S, Regberg A, Serenius S, Enocson A.
The Journal of Bone and Joint Surgery. 2019;101(13):1168-1176.

III. EPIDEMIOLOGY, CLASSIFICATION, TREATMENT AND MORTALITY OF DISTAL RADIUS FRACTURES IN ADULTS: AN OBSERVATIONAL STUDY OF 23,394 FRACTURES FROM THE NATIONAL SWEDISH FRACTURE REGISTER
Rundgren J, Bojan A, Mellstrand Navarro C, Enocson A.
BMC Musculoskeletal Disorders. 2020;21(1):88.

IV. SURGICAL SITE INFECTIONS AFTER DISTAL RADIUS FRACTURE SURGERY: A NATION-WIDE COHORT STUDY OF 31,807 ADULT PATIENTS
Rundgren J, Enocson A, Järnbert-Pettersson H, Mellstrand Navarro C.
Manuscript submitted.

CONTENTS

LIST OF ABBREVIATIONS

AO/OTA	Arbeitsgemeinschaft für Osteosynthesefragen/Orthopedic Trauma Association
ASA	American Society of Anesthesiologists physical status classification system
ATC	Anatomical Therapeutic Chemical classification
AUROC	Area Under ROC curve
CDC	Centers for Disease Control and Prevention
CI	Confidence Interval
CONSORT	Consolidated Standards of Reporting Trials
DASH	Disabilities of Arm, Shoulder and Hand questionnaire
DRF	Distal Radius Fracture
EC	External Criterion
EF	External Fixation
EQ-5D	EuorQol group-5 Dimensions
EQ-5D-3L	EuorQol group-5 Dimensions-3 Levels
GA	General Anesthesia
ICD-10-SE	International statistical Classification of Diseases and related health problems 10th revision, Swedish version
IQR	Interquartile Range
IV	Intravenous
HRQoL	Health-Related Quality of Life
MID *or* MIDC	Minimal Important Difference *or* Minimal Clinically Important Difference
NCSP-S	NOMESCO Classification of Surgical Procedures, Swedish version
NOMESCO	Nordic-Medico-Statistical Committee
NPR	Swedish National Patient Register
NSAID	Non-Steroidal Anti-Inflammatory Drug
OEC	Opioid Equivalent Consumption
OR, aOR	Odds Ratio, adjusted Odds Ratio
ORIF	Open Reduction with Internal Fixation
PACU	Post-Anesthesia Care Unit
PO	Peroral

PONV	Postoperative Nausea and Vomiting
PRO	Patient-Reported Outcome
PROM	Patient-Reported Outcome Measure
PRWE	Patient-Rated Wrist Evaluation
PRWE-Swe	PRWE, Swedish version
QALYs	Quality-Adjusted Life-Years
RA	Regional Anesthesia
RCT	Randomized Clinical (or Controlled) Trial
ROC	Receiver Operating Characteristic curve
SD	Standard Deviation
SES	Standardized Effect Size
SF-36	36-item Short Form health survey questionnaire
SFR	Swedish Fracture Register
SPDR	Swedish Prescribed Drug Register
SRM	Standardized Response Mean
SSI	Surgical Site Infection
VAS	Visual Analog Scale

INTRODUCTION

DEFINITION

A distal radius fracture (DRF) is defined in this thesis as a fracture of the distal end of the radius, with or without a concomitant fracture of the most distal part of the ulna, i.e. the styloid process.

EPIDEMIOLOGY

The DRF is the most common fracture type treated in the health-care system.[1] With an incidence rate of 32/10,000 person-years in the total population, it afflicts about 32,000 persons in Sweden each year.[2] The fracture distribution (both prevalence and incidence) in the total population is bi-modal with a first peak primarily in boys and young male adolescents, and a second peak in women 50 years or older.[1-5]

A few region-specific studies have suggested both seasonal and weekly variations in DRF incidence in Finland,[6] Norway,[7] the United states,[8] and the United Kingdom.[5]

The previous literature has been lacking nation-wide epidemiological studies providing comprehensive data on patient- and injury-related characteristics, fracture classification, as well as mortality of DRFs.

ETIOLOGY

The most common cause of injury is a fall on an outstretched arm with a dorsally extended hand.[9] A majority of DRFs in younger adults are due to a high-energy trauma mechanism,[10] while in middle-aged and elderly patients, a low-energy trauma mechanism, such as a fall from a standing position, is most common.[11] There is a well-established association between DRFs in post-menopausal women and a reduced bone mineral density.[12-14] In a study of women aged 55 to 80 years sustaining a DRF, the occurrence of osteopenia and osteoporosis was 85% and 51% respectively.[15]

CLASSIFICATION

The nomenclature used for describing DRFs has evolved over time. Today numerous classification systems for DRFs exist, neither of which have been unanimously accepted.[16,17] One of the most frequently used is the AO/OTA (Arbeitsgemeinschaft für Osteosynthesefragen/Orthopedic Trauma Association) classification system for orthopedic fractures, which is based on the localization and morphology of the fracture.[18] In **Figure 1**, a schematic overview of the AO/OTA classification system for DRFs is presented. Further, more archaic terminologies for DRFs are still widely used. These include the Colles eponym referring to an extra-articular metaphyseal DRF with dorsal displacement of the distal fragment,[19] the Barton eponym referring to a partial intra-articular DRF,[20] and the Smith eponym referring to a DRF with volar displacement of the distal fragment.[21]

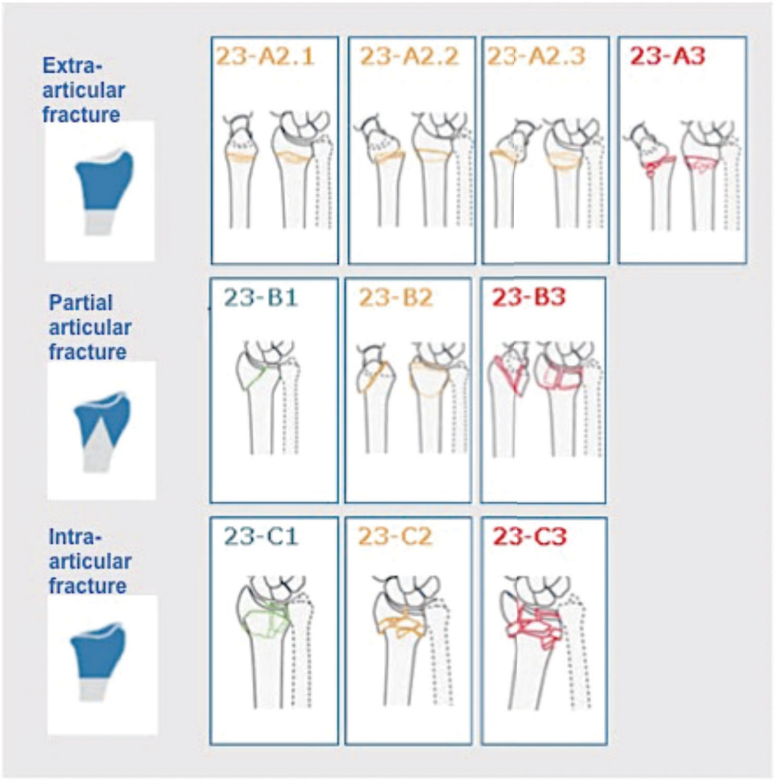


Figure 1. *Schematic overview of the AO/OTA classification system for DRFs.*

TREATMENT OPTIONS

Treatment of a DRF may vary from elastic bandage to complex open surgery and is dependent on fracture- and patient-related factors. Further, current trends, as well as the treating surgeon's and the patient's preferences may also influence treatment decision.

Non-surgical treatment

Approximately 80% of all DRFs are treated non-surgically.[2] The most common type of non-surgical treatment is immobilization with a short-arm cast for 4 to 6 weeks, preceded by closed reduction if necessary.[22,23] Radiologic and clinical assessment is usually performed after 8 to 14 days, with the main purpose of detecting fractures subject to loss of reduction, and in need of surgery.

Surgical treatment

Surgical treatment is predominantly used for DRFs with unacceptable intra-articular displacement (≥ 2 mm step-off) and/or fracture instability, i.e. an inherent inability to retain the fracture position after closed reduction. Factors associated with fracture instability and the subsequent loss of reduction include high age, dorsal comminution, initial dorsal tilt > 20 degrees, loss of radial length, intra-articular involvement and a concomitant ulna fracture.[17,24-26]

The main methods used in DRF surgery in adults include: open reduction with internal fixation (ORIF) using a volar plate, closed reduction with percutaneous pinning, and closed reduction with external fixation. Combinations of these methods may be used when appropriate. After fracture healing, the external fixator and/or pins are removed, usually within 4-6 weeks, in an out-patient setting. Removal of internal fixation hardware is not routinely done, but may be necessary if postoperative complications arise.

Previous studies have reported that longer-term (> 3 months) functional and patient-reported outcomes are similar between the main surgical methods.[27-32]

Over the last two decades, there has been a considerable shift in treatment trends; the proportion of surgically treated DRFs have gradually increased, and the preferred surgical method has changed from percutaneous methods to ORIF.[2,4,33-38]

ANESTHESIA IN DISTAL RADIUS FRACTURE SURGERY

Most adult patients with a DRF in need of surgery can be treated in a day surgery setting. Anesthesia during DRF surgery is achieved with either general anesthesia (GA) or regional anesthesia (RA), frequently in the form of a brachial plexus blockade. These anesthesia methods differ with regard to technique, benefits, spectrum of associated side effects and complications, as well as in perioperative time consumption and health-care resources needed.[39] In ambulatory shoulder surgery, previous studies have reported that RA with a brachial plexus blockade provides greater hemodynamic stability and muscle relaxation during surgery, improved intra- and postoperative analgesia, decreased opioid requirements, reduced postoperative anesthesia care resource consumption, decreased number of unplanned admissions for pain control and improved patient satisfaction, compared to GA.[40,41]

Although DRF surgery is frequently performed, the authors of a recent review of the available literature assessing GA, RA or a combination of these, for open wrist surgery in adults, with regard to early postoperative pain and longer-term outcomes, identified only a few existing studies, which were of varying quality and had conflicting results.[42] The authors concluded that the evidence was too sparse to decide on the superior anesthesia method and recommended further studies.

COMPLICATIONS AFTER SURGICAL TREATMENT

Well-known complications following DRF surgery include: tendon-related problems (tenosynovitis and ruptures), nerve injuries, fracture malunion, posttraumatic osteoarthritis, complex regional pain syndrome and surgical site infection (SSI).[43-46] The spectrum and frequency of associated complications vary considerably between the main surgical methods.[43-47] Further, patient factors such as health status, life style, age and social support may also influence the risk of complications.[44] Thus, it is of great importance that surgeons treating patients with a DRF have knowledge of the complications associated with each treatment method, as well as associated risk factors, in order to achieve the most favorable outcome for all patients.

Surgical site infection (SSI)

SSI (i.e. postoperative infection or infection after fracture fixation) is a feared complication in orthopedic trauma surgery. Factors influencing the development of an orthopedic SSI include severity of the fracture, fracture type (open/closed), status of the surrounding soft tissues, type of contaminating pathogens and the patient's health status.[48,49] Not only may SSIs result in delayed healing, functional loss and protracted recovery periods,[48] but they also cause a significant additional economic cost to the health-care system.[50]

There is a lack of consensus in the literature regarding standard criteria and definition of SSI.[48] The American Centers for Disease Control and Prevention (CDC) have provided a frequently cited definition based on depth of tissue involvement at diagnosis which subdivides SSIs into: superficial incisional, deep incisional and organ space.[51] According to the CDC classification, an SSI must occur within 30 days of surgery, unless a foreign material has been implanted, in which case the time frame is one year. A widely used classification scheme which has proved clinically relevant in the treatment of infections after fracture fixation classifies SSIs based on the time of onset after surgery: early (< 2 weeks), delayed (2-10 weeks) and late (> 10 weeks).[52] Early onset orthopedic SSIs are primarily caused by the high-virulence pathogen Staphylococcus aureus, presenting with classic symptoms of infection (swelling, redness, pain, secretion and/or pus), while later onset SSIs are primarily caused by low-virulent bacteria capable of producing biofilm, such as Staphylococcus epidermidis, often presenting with more subtle symptoms.[48,49]

With regard to DRF surgery, most SSIs are superficial, e.g. pin site infections in patients treated with percutaneous pinning or external fixation, and can be managed with peroral antibiotics.[30,44] However, if not treated promptly, they may develop into a deep SSI with subsequent osteomyelitis and non-union, which requires in-patient care with intravenous antibiotics and repeated surgical site debridements.[44] Previous data on the rate of SSIs after DRF surgery is based on retrospective case series without a comparator, and small prospective clinical studies in which SSI was studied as a secondary outcome.

EVALUATION OF TREATMENT OUTCOME

Traditionally, the evaluation of treatment outcome after musculoskeletal injuries has included radiologic assessment, functional outcomes (range of motion and grip strength) and frequency of complications.[53] However, theses outcomes do not always correspond to the patient's own assessment of treatment outcome.

Patient-reported outcome measures (PROMs)

In recent decades the use of PROMs has greatly increased in health-care practice, and they now play an important role in the evaluation and comparison of health-care interventions. A health-related PROM is an instrument designed to measure patient-reported outcomes (PROs), i.e. any aspect of a patient's health status including pain, functional status and health-related quality of life (HRQoL).[54] PROMS provide patient-reported information unfiltered by an observer or physician. PROMs can be either specific or generic (general). A specific PROM is designed to detect changes in PROs in a specific patient group, such as a defined disease, injury, treatment or anatomical region. Two examples of region-specific PROMs

relevant to this thesis include the Patient-Rated Wrist Evaluation (PRWE) specific for the wrist,[55] and the Disabilities of Arm, Shoulder and Hand questionnaire (DASH) specific for the upper extremity.[56] Contrary, generic PROMs measure PROs not related to a specific injury, disease or treatment. While they allow comparisons between different patient groups, an inherent disadvantage is that they are less sensitive to capture small changes in PROs. Two well-known examples of generic PROMs measuring general HRQoL include the EuroQol Group 5-Dimension (EQ-5D),[57-60] and the 36-item short form health survey (SF-36).[61,62]

Important measurement properties of PROMs

Health-related PROMs are widely used in clinical practice and scientific research, and the results often guide treatment decisions.[54] The constructs (PROs) that they are designed to measure, e.g. pain, functional status and HRQoL, are of a subjective nature. Thus, before a PROM is applied in any patient group, its measurement properties must be assessed and deemed adequate. Relevant measurement properties of PROMs have been categorized into three domains: reliability, validity and responsiveness.[54]

Reliability and validity

Reliability refers to the extent to which the PROM is free from measurement error, i.e. is able to provide consistent and reproducible results, and encompasses internal consistency, test-retest stability, inter-rater and intra-rater stability, as well as random error. Validity refers to the extent to which an instrument measures the construct it is designed to measure. Properties of validity are content validity, construct validity and criterion validity.[54]

Responsiveness

Responsiveness refers to an instrument's ability to detect clinically relevant change over time in the construct to be measured, reflected by a proportional change in the instrument's scale.[54,63] It encompasses internal responsiveness, which refers to the instrument's ability to detect a hypothesized change over time, and external responsiveness, which refers to the instrument's ability to correlate to an external criterion (EC). The EC is another instrument used as a gold standard, with ascertained validity, reliability and responsiveness for the intended patient group.[63]

If a PROM is used in a patient group for which its responsiveness has not been tested or is insufficient, the risk of drawing faulty conclusions based on the score results is large, due to the uncertain or insufficient ability of the instrument to correctly capture the change in health status that actually takes place in the patients.

Further aspects

An important characteristic of PROMs is interpretability, which refers to the extent to which qualitative clinical meaning can be assigned to an instrument's quantitative scores or change in scores. It is affected by several factors, including: response burden, i.e. the number of questions that the patient is requested to answer, which has implications on the response rate; floor and ceiling effects, i.e. the proportion of patients in a study population reporting the highest or lowest possible score; the distribution of scores and score changes; and Minimal

Important Difference (MID), defined as the smallest change in an instrument's score which by patients is considered a relevant clinical change. The MID is specific to different PROMs and patient groups.[64]

AIMS

The overall aim of this thesis was to contribute to a more evidence-based care for adult patients with a DRF by investigating aspects of epidemiology, surgical management and treatment outcome evaluation.

The specific aims of the included studies were:

STUDY I
To assess the internal and external responsiveness of EQ-5D (specifically EQ-5D-3L index score) in adults with a surgically treated DRF, i.e. to investigate its ability to detect clinically relevant change in HRQoL in adult patients recovering after surgical treatment of an acute DRF. PRWE-Swe was used as the external criterion.

STUDY II
To compare regional and general anesthesia in adults with a DRF treated with volar plate fixation in a day surgery setting with regard to early postoperative opioid consumption and pain, perioperative time consumption, as well as wrist function and PROMs at 6 months.

STUDY III
To describe the epidemiology, fracture classification, injury characteristics, current practice and mortality of DRFs in the adult Swedish population.

STUDY IV
To assess the rate of surgical site infections after plate fixation, percutaneous pinning and external fixation of DRFs in the adult Swedish population, and to study factors associated with a surgical site infection.

MATERIALS AND METHODS

ETHICAL APPROVAL

All studies included in this thesis were conducted according to the Helsinki declaration,[65] and were ethically approved; Study I, II and IV were approved by the Regional Ethical Review Board of Stockholm, and Study III by the Swedish Ethical Review Authority.

SETTING AND DATA SOURCES

All studies included in this thesis were performed in Sweden. The study populations were derived either from patients presenting at the Södersjukhuset (South General Hospital) in Stockholm, or from population-based health-care registers.

The Södersjukhuset in Stockholm is a level-II trauma center with a large catchment area. The number of unique visits at the hospital's Emergency departments in 2019 was 140,307.[66] The inflow of patients with an acute DRF to the Orthopedic department is voluminous and, apart from patients presenting at the Emergency department, also includes patients referred from primary care emergency walk-in units to the Orthopedic out-patient clinic for assessment, treatment and follow-up.

Sweden has a tax-funded public health-care system available to all residents based on need. There is a long tradition of monitoring the population by collecting sociodemographic data in Sweden. The Swedish National Board of Health and Welfare has been instrumental in the development and management of several population-based health-care registers. Participation is mandatory for health-care providers, granting a high coverage.

Further, in the last decades several national quality registers for specific diagnoses and treatments have been developed with the purpose of monitoring outcome, facilitating research and improving future treatment. Although registration in these registers is not mandatory, they provide important data sources.

Since 1947, all Swedish residents are assigned a unique personal identity number at birth or on a residence permit. This provides a key by which information from different registers may be linked, enabling population-based epidemiological studies with combined data.

The Swedish national patient register (NPR)

The NPR is maintained by the Swedish National Board of Health and Welfare.[67] National coverage of public in-patient care was achieved in 1987. Registration of surgical interventions became mandatory in 1993, followed by day-care surgery in 1997 and other hospital-based out-patient care in 2001. Private caregivers have been included since 2001. The information registered in the NPR is comprehensive and includes patient-related data, data about the caregiver, administrative data and medical data including codes for main and secondary diagnoses and surgical procedures. Patients' diagnoses are coded according to the Swedish version of the International statistical classification of diseases and related health problems 10th revision (ICD-10-SE) system. Surgical procedures are coded according to the Swedish version of the Nordic-Medico-Statistical Committee (NOMESCO) Classification of Surgical Procedures (NCSP-S).[68]

The coverage of in-patient care registrations, including surgery, is 99%, with a drop-out rate for the main variables of 1% since 1987.[69,70] A previous review of 132 papers investigating the external validity of in-patient diagnose registrations found a high validity for many diagnoses and an overall positive predictive value of 85-95%.[70] For hospital-based out-patient care the data quality has improved greatly since 2001, with a decrease in drop-out rate for the main variables from 25-30% to about 3%.[69]

The Swedish prescribed drug register (SPDR)

The SPDR is maintained by the Swedish National Board of Health and Welfare.[71] The register provides detailed data on all prescribed drugs dispensed in Swedish pharmacies, including Anatomical Therapeutic Chemical (ATC) classification codes, dates of prescription and dates of dispensation. Since July 2005, the SPDR includes personal identity numbers, thus allowing linkage to other registries.

The Swedish fracture register (SFR)

The SFR is a national quality register for orthopedic fractures and treatments which started in 2011.[72] Registered data include patient and fracture characteristics, injury mechanism and fracture treatment. Fractures are classified according to the AO/OTA classification system.[18] Previous studies have shown that the fracture classification data for several fracture types has a high accuracy and validity.[73-76] The SFR is linked to a death register managed by the Swedish Tax Agency, from which data on patient mortality can be obtained. Previous studies of specific fracture types based on data from the SFR include humeral, clavicle, tibial and proximal femoral fractures.[77-80]

Patient-reported outcome measures (PROMs) relevant to the thesis

EQ-5D (specifically EQ-5D-3L)

The original 3-level version of EQ-5D (EQ-5D-3L) is a well-known and established PROM designed to measure general HRQoL.[57-60] It essentially consists of the EQ-5D-3L questionnaire (i.e. descriptive system) and the EQ visual analog scale (EQ-VAS). In this thesis, the EQ-5D-3L questionnaire was used. It is designed so that the respondent classifies his/her general health according to 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension is graded by the respondent into one of three levels: 1, no problems; 2, some or moderate problems; or 3, extreme problems, hence the name EQ-5D-3L.

The 5-digit result of the EQ-5D-3L questionnaire (e.g. 22131) represents one of 243 (5^3) possible health states. As these health states do not have identical impact (weight) on patients' HRQoL, specific HRQoL weights have been constructed for each unique health state, i.e. a value set. In this thesis, a widely used value set based on a large population sample from the United Kingdom (UK), the UK EQ-5D Index Tariff, was used.[81,82] By applying the weights from this value set, each health state is converted into a single summary index score (EQ-5D index score) ranging from -0.594 to 1.00. For practical purpose, all negative index scores through 0.00 were classified as 0.00, representing the worst possible health state, while 1.00 represent the best possible health state. The MID for the EQ-5D index

score was set to 0.1, based on previous studies.[83] An important application of EQ-5D is health-economic evaluation, for which it is commonly used as an estimate of the HRQoL component (utility, i.e. effect) in quality-adjusted life years (QALYs). QALYs are used in cost-effectiveness analyses, which may guide resource allocation on a population level.[84]

Patient-Rated Wrist Evaluation (PRWE)

The PRWE is a PROM specific to the wrist, which is designed to measure patient-reported wrist pain and disability in activities of daily living.[55] It has proved to be valid, reliable and responsive.[85,86] The PRWE is a 15-item questionnaire consisting of a pain subscale with 5 items and a function subscale with 10 items. The patient rates his/her level of wrist pain and function on a categorical scale from 0 to 10, where 0 equals no pain/no difficulty, and 10 equals worst pain ever/unable to do. The scores of the 5 pain subscale items are summed and can thus be 50 at worse. The scores of the 10 function subscale items are summed and divided by 2, and thus equals 50 at worse as well. The result of the PRWE is the sum of these scores, i.e. a number between 0 and 100, where 0 represents a fully functioning and painless wrist and 100 represents a completely disabled and extremely painful wrist. The MID for PRWE was set to 10 points based on previous studies.[86] In this thesis, the Swedish version of the original PRWE, the PRWE-Swe, was used. It has proved good validity, reliability and responsiveness in a Swedish setting.[87,88]

STUDY I

Study design

Within the context of a previous RCT, the internal and external responsiveness of EQ-5D index score was assessed using PRWE-Swe as an external criterion (EC).

Study population

A total of 1349 consecutive patients (age 50-74 years for women and 60-74 years for men) with a dorsally displaced DRF scheduled for surgical treatment at the Södersjukhuset between September 2009 and February 2013 were eligible for inclusion in the previous RCT. 140 patients were included and randomized to either volar plate fixation or external fixation.[31] One patient was excluded momentarily after randomization due to fracture misclassification, leaving 139 patients for 12 months follow-up in the RCT. In Study I, a total of 132 of these patients were included, all of which had completed the relevant questionnaires at all 3 measuring points. The process of inclusion and exclusion of the study population in Study I is visualized in **Figure 2**.

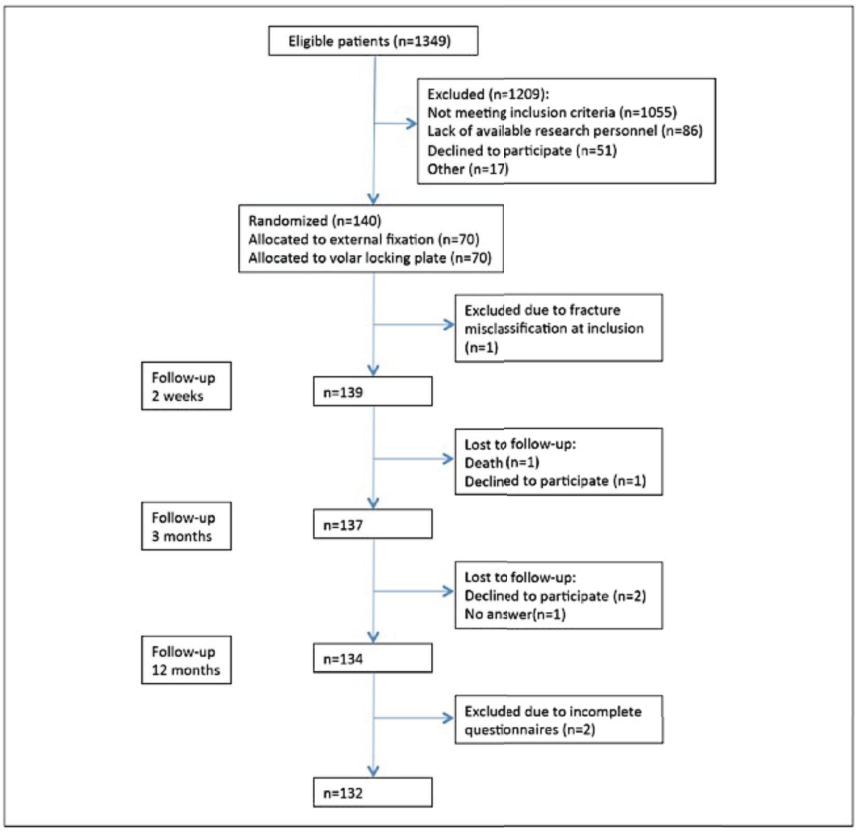


Figure 2. *Flowchart of the inclusion and exclusion process of Study I.*

Methods and statistical analysis

In Study I, fully completed EQ-5D and PRWE-Swe questionnaires at baseline (recall of the week before injury), at 3 months and 12 months postoperatively of 132 patients participating in the RCT were analyzed. Demographic data was collected from study protocols and patients' charts.

Scale compatibility

EQ-5D scores were converted to EQ-5D index scores using the UK value set.[81,82] To enable comparison between the EQ-5D index scores and PRWE-Swe scores, both scoring scales were adjusted so that the best scores (most positive health state) equaled 100.

Hypothesis for assessment of internal and external responsiveness

As none of the included patients suffered from wrist disability prior to injury we hypothesized that all patients would report a substantial deterioration in EQ-5D index score and PRWE-Swe score at 3 months compared to the preinjury state. Further, we hypothesized that most patients would report an increase (major or minor) in EQ-5D index scores and

PRWE-Swe scores from the 3-month to the 12-month follow-up. However, a subgroup of patients was expected to report further deterioration at the 12-month follow-up.

Assessment of internal responsiveness

To assess the internal responsiveness of the EQ-5D index score, i.e. it's ability to detect the hypothesized change in HRQoL over time, the mean change score (observed change) and the standardized response mean (SRM), defined as the mean change score divided by the standard deviation (SD) of the change score, from baseline to the 3-month follow-up, and from the 3- to the 12-month follow-up was calculated. The SRM was classified as large (>0.8), moderate (0.5-0.8) or small (<0.5).[83,89]

Assessment of external responsiveness

The external responsiveness of the EQ-5D index score was evaluated by how well it corresponded to the changes captured by the PRWE-Swe, which was used as the EC. The PRWE-Swe change scores from the 3- to the 12-month follow-up were used to discriminate between 4 subgroups of patients with separate clinical outcomes: clearly improved, with an increase in change score of ≥10 points; marginally improved, with an increase in change score of <10 points; marginally deteriorated, with a negative change score of <10 points; and clearly deteriorated, with a negative change score of ≥10 points. The cutoff level of 10 points was chosen based on the MID for PRWE.[86] Thus, after adjustments for scale compatibility, the MID for both PRWE-Swe and EQ-5D index score was 10 points.

Statistical analyses of external responsiveness included Receiver Operating Characteristic (ROC) curves used to evaluate the ability of the EQ-5D index change score between the 3- and 12-month follow-ups to discriminate between the 4 subgroups defined by the EC, providing information on the specificity and sensitivity of the EQ-5D index change scores. Arean Under ROC curves (AUROCs) were analyzed and correlated to the probability of correctly identifying patients in the 4 subgroups defined by the EC. AUROCs may range from 0.5 (no discriminatory accuracy) to 1.0 (perfect accuracy). The EQ-5D index score was hypothesized to have the ability to significantly discriminate between the 4 subgroups defined by the EC. To ensure a clinically relevant difference between the reference and comparison groups, comparisons were made between subgroups with a difference of ≥10 points in the EC. A logistic regression analysis was performed in which odds ratios (ORs) were calculated with the EC as the dependent variable and the EQ-5D index change score as the independent variable. The patient group with the more favorable outcome was used as the reference. An OR exceeding 1.0, thus indicated that the odds of belonging to the group with the less favorable outcome increased among patients with a comparatively worse EQ-5D index score. Further, the proportion of patients correctly classified by EQ-5D index change scores into the 4 subgroups defined by the EC was assessed. We predicted it to be larger than 50%, which is the proportion expected by chance. Finally, a correlation analysis of the EQ-5D index change score and PRWE-Swe change score between the 3- and the 12-month follow-ups was performed, using the Spearman's ρ test, for which a positive direction of the correlation and a strength of the coefficient ≥0.30 was predicted.

STUDY II

Study design

Study II was a pragmatic single-center randomized clinical trial (RCT), adhering to the Consolidated Standards of Reporting Trials (CONSORT) guidelines.[90]

Study population

Assessed for eligibility were all patients planned for volar plate fixation of a displaced DRF in orthopedic day surgery at the Södersjukhuset in Stockholm, between March 23rd 2015 and November 9th 2016. Inclusion criteria were age 18-74 years, residency within the Stockholm area, adequate comprehension of Swedish and the occurrence of a DRF within 16 days prior to surgery. Exclusion criteria were a concomitant ulnar fracture proximal to the base of the styloid process, a complex DRF requiring auxiliary osteosynthesis, previous ipsilateral wrist or hand dysfunction, previous pain disorder, concomitant nerve, tendon, or skin injury in the fractured wrist, concomitant notable injuries requiring additional surgery and/or pain medication, drug or alcohol abuse, severe psychiatric disorder, systemic inflammatory disease, or a medical condition making either method of anesthesia inappropriate. A total of 305 patients were assessed for eligibility, of which 90 patients were included and randomized. Two patients not meeting the age criteria were included by mistake and had to be excluded after randomization, leaving a total of 88 patients for follow-up. A CONSORT flowchart is presented in **Figure 3**.

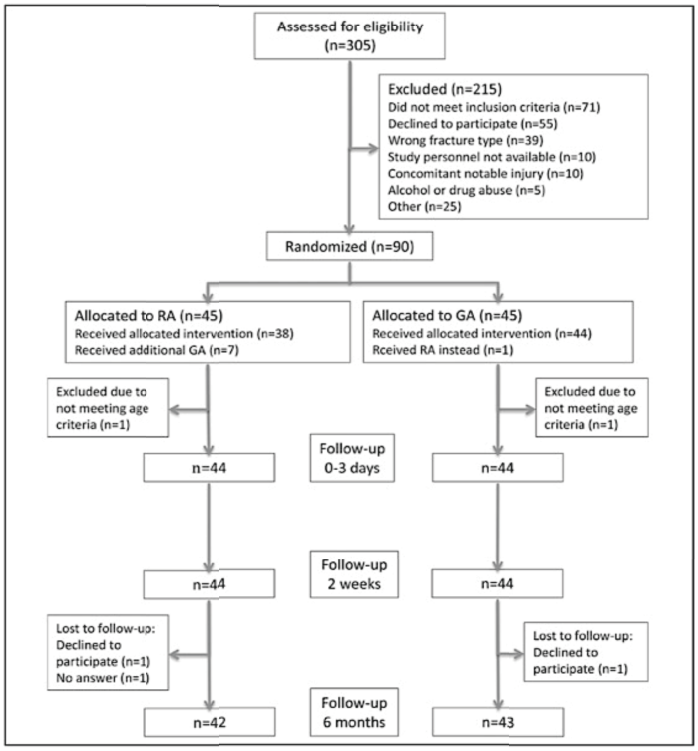


Figure 3. *CONSORT flowchart of Study II.*

Interventions

The study protocol was pragmatic in the sense that it adhered to the hospital's clinical routines regarding anesthetic and surgical interventions, postoperative care and follow-up, and that no specific study personnel was appointed to perform the interventions. After written informed consent, patients were randomized to either RA or GA.

Regional anesthesia (RA)

A single-shot supraclavicular plexus blockade was administered by an anesthesiologist with ultrasound guidance in an anesthesia care preparation area. It consisted of a mixture of mepivacaine (10 mg/mL) and levobupivacaine (2.5 mg/mL), two-thirds to one-third, with a total dose of approximately 20 mL, individually adjusted at the discretion of the anesthesiologist.

General anesthesia (GA)

GA was performed in the operating theatre by a trained anesthesiology nurse. Propofol and fentanyl were used to induce GA, and sevoflurane and fentanyl to maintain it. Individual doses were left to the discretion of the anesthesiology team. All GA patients were administered 4 mg betamethasone IV to prevent postoperative nausea and vomiting (PONV). After wound closure, the surgeon administered 10 mL levobupivacaine (5 mg/mL) at the surgical site in GA patients.

Premedication, surgery and postoperative care

Preoperatively, all patients received the same peroral premedication in the orthopedic ward, including the following analgesics and antiemetic medication: acetaminophen (2 x 665 mg), oxycodone (5 or 10 mg), etoricoxib (90 mg; if no contraindication), and meclizine (25 mg).

All patients underwent surgery with a standard volar approach to the distal radius, followed by ORIF with a volar locking plate. The exact type of implant was left to the discretion of the appointed surgeon. A dorsal plaster cast was applied for 2 weeks postoperatively.

Postoperatively, patients receiving RA were taken directly to the orthopedic ward, while patients receiving GA were transferred to the post-anesthesia care unit (PACU) for observation and pain-relief, before returning to the orthopedic ward. Prior to discharge, all patients were prescribed analgesics for postoperative pain, but the type and dose were left to the discretion of the treating surgeon.

Outcomes

The primary outcome was the total opioid equivalent consumption (OEC) during the first 3 postoperative days (72 hours).

The secondary outcomes included: OEC before and after discharge during day 1, and OEC during days 2 and 3; pain as measured with a visual analog scale (VAS, 0-10) preoperatively, immediately postoperatively, at 2 hours postoperatively, at discharge, at 24, 48 and 72 hours, at 2 weeks, and at 6 months postoperatively; the timing and intensity of the postoperative pain peak; PONV in the first 24 hours postoperatively (yes/no and VAS, 0-10); perioperative

time consumption (surgical, preoperative and postoperative anesthesia care time); and functional outcomes (range of motion and grip strength) and PROMs (EQ-5D-3L and PRWE-Swe) at 6 months.

Data on opioid consumption and conversion to opioid equivalents

Information on type and dose of analgesics administered postoperatively in the PACU and/or the orthopedic ward before discharge was collected from patients' charts. Patients noted the type, dose and time of all analgesics consumed after discharge during the first 3 postoperative days in a protocol handed to them before discharge. One of several members of the study team, not blinded to the intervention, contacted the patients via telephone daily during the early postoperative period for a report on analgesic intake and other relevant outcomes. All opioid analgesics were converted to opioid equivalents (mg of PO morphine) using established equianalgesic conversion tables.[91]

Statistical analysis

A power analysis was performed before study commencement. The power was set to 80% and the significance level to 0.05. The MID in total mean OEC during the first 3 postoperative days between the two groups was set to 10 mg ± 15 SD, based on a pilot case series and our clinical experience. The dropout rate was assumed to be 5 patients per group. Based on the above, the sample size was set to 90 patients.

Results were analyzed according to the intention-to-treat principle. The Shapiro-Wilks test was used to test normality. Nonparametric variables were compared using the Mann-Whitney U test. Variables with normal distribution were compared using the Student t test. Nominal variables were assessed with the Fisher exact test. All tests were 2-sided. Results were considered significant at $p<0.05$.

STUDY III

Study design

This was a nation-wide observational descriptive cross-sectional register study, comprising a 3-year time period.

Study population

Included were all non-pathological DRFs in patients aged 18 years or older registered in the SFR between January 1st 2015 and December 31st 2017. Excluded were all re-fractures, defined as a new fracture in the same wrist within 60 days. A total of 23,394 DRFs in 22,962 patients were identified.

Variables

The variables studied were patient-related (age, sex), injury-related (injury location, cause, date), fracture-related (fracture classification, side, open/closed, high-/low-energy trauma mechanism), and treatment-related (primary treatment type, surgical method, secondary surgery). Injury location was categorized into: in the patient's residence or accommodation

(including institutional housing), in a street/road, in a public place, or in an unspecified place. Injury cause was categorized into: a simple fall (i.e. a fall in the same level), a fall from height, an unspecified fall, a traffic accident or any other cause. Fractures were classified according to the AO/OTA classification system and the ICD-10-SE code system. Primary treatment type was categorized into: primary non-surgical or primary surgical. The primary surgical treatment was further categorized into: plate fixation, external fixation, pin/wire fixation, or any other method. DRFs primarily treated non-surgically but with a secondary operation within 28 days were identified. Lastly, patient mortality was calculated and presented as 30-day and 1-year mortality.

Statistical analysis

Nominal variables were presented as proportions (%) of all registered fractures (i.e. the available number of inputs in the SFR data file excluding any missing values). Scale (continuous) variables were presented as means ± SDs.

STUDY IV

Study design

This was a nation-wide observational cohort study linking prospectively registered data from two Swedish population-based health-care registers (the NPR and the SPDR).

Study population

Included in this study were all patients aged 18 years or older with a surgically treated DRF registered in the NPR between November 1st 2006 and October 31st 2013. A DRF was defined as a registration of the ICD-10-SE codes S525 or S526. The included surgical methods were defined as a registration of the following NCSP-S codes: NCJ29, NDJ29 = external fixation, NCJ49, NDJ49 = percutaneous pinning, NCJ69, NDJ69 = plate fixation. The date of surgery (index date) was defined as the first registration of a relevant surgical procedure code (NCJ29, NDJ29, NCJ49, NDJ49, NCJ69 or NDJ69) with a concomitant relevant DRF code (S525 or S526), occurring within 28 days of the "first DRF registration" in the NPR. A "first DRF registration" was defined as the occurrence of a DRF code preceded by a period of at least 18 months without any DRF registration in the NPR. If a patient had several index dates during the study period, only the first index date (i.e. the first surgical treatment) was included. Concomitant bilateral fractures were analyzed as one unilateral fracture. Thus, each unique patient was only included once, and the number of DRFs in the analysis equals the number of patients. A total of 31,807 patients were identified and included in the analysis.

Exposures

Included patients were allocated to either of three exposure groups based on surgical method: plate fixation, percutaneous pinning or external fixation.

Primary outcome

The primary outcome was a registration in the SPDR of a dispensed prescription of peroral Flucloxacillin and/or Clindamycin within the first 8 weeks following DRF surgery (yes/no), which was used as a proxy for a surgical site infection (SSI). The ATC codes for Flucloxacillin (J01CF05) and Clindamycin (J01FF01) were used to identify the drugs in the SPDR.

Potential confounders

Potential confounders included age, sex, fracture type (closed/open), and a dispensed prescription of Flucloxacillin and/or Clindamycin during the 8 weeks preceding DRF surgery.

Statistical analysis

Data were presented as numbers and percentages for the three surgical methods, respectively. Logistic regression was used to study the association between surgical method and the primary outcome, adjusted for potential confounders. Odds ratios (ORs) were presented with a 95% confidence interval (CI) and a corresponding p-value. The results were considered significant at $p<0.05$ in 2-sided tests. Classification tree analysis, adjusted according to Bonferroni, was used to study which factors were associated with the primary outcome.

OVERVIEW OF THE STUDIES INCLUDED IN THE THESIS

	Study I	Study II	Study III	Study IV
Design	Within the context of a previous RCT, the responsiveness of EQ-5D index score was assessed	Single-center pragmatic RCT	Nation-wide descriptive cross-sectional study	Nation-wide cohort study
Population	Patients aged 50-74 years undergoing surgical treatment of a DRF at the Södersjukhuset	Patients aged 18-74 years undergoing plate fixation of a DRF in day surgery at the Södersjukhuset	Non-pathological DRFs in patients aged 18 years or older	Patients 18 years or older with a surgically treated DRF
Study period	Sep 2009-Feb 2013	Mar 2015-Nov 2016	Jan 2015-Dec 2017	Nov 2006-Oct 2013
Number in analysis	132 patients	88 patients	23,394 DRFs in 22,962 patients	31,807 patients
Follow-up time	12 months	6 months	No follow-up	8 weeks
Data sources	Patients' charts, study protocols	Patients' charts, study protocols	SFR	NPR, SPDR
Intervention	Plate fixation or EF	RA or GA	Not applicable	Not applicable
Exposure	Not applicable	Not applicable	Not applicable	Surgical method
Main outcomes	Internal and external responsiveness of EQ-5D index score in patients with a DRF. PRWE-Swe was used as the external criterion	Early postoperative OEC (Day 1-3), VAS for pain and PONV. Perioperative time consumption. Functional outcomes and PROMs at 6 months	Patient-, injury-, fracture- and treatment-related distribution data	A dispensed prescription of Flucloxacillin and/or Clindamycin within the first 8 weeks following DRF surgery (a proxy for an SSI), and factors associated with an SSI
Main statistical methods	Mean change scores, SRMs, AUROCs, logistic regression, correlation analysis	Shapiro-Wilk test, Mann-Whitney U test, Student t test, Fisher exact test	Numbers and proportions, means with SDs	Logistic regression, Classification tree analysis

RESULTS

STUDY I

The results from Study I showed that the EQ-5D index score had an overall good internal responsiveness and an acceptable to good external responsiveness in patients with a surgically treated DRF.

Good internal responsiveness was supported by statistically significant mean change scores of the EQ-5D index score between preinjury state and the 3-month follow-up (-16.1; SD 17.4, $p<0.001$) and between the 3- and the 12-month follow-ups (7.6; SD 16.2, $p<0.001$), with corresponding large (0.93; 95% CI 0.75-1.10) and small to moderate (0.47; 95% CI 0.30-0.64) SRMs.

Overall results of the subgroup analyses for the external responsiveness showed an acceptable correspondence of the EQ-5D index score to the EC.

In **Table 1**, the results from the ROC curve analysis and logistic regression analysis are presented. The AUROCs ranged from 0.70 to 0.76 with CIs above 0.5 for all but one group, indicating a good ability of the EQ-5D index score to discriminate between different outcomes in patients with a surgically treated DRF. Logistic regression displayed statistically significant ORs exceeding 1.00 for all groups. The proportion of patients correctly classified by EQ-5D index change scores into the 4 subgroups defined by the EC was 78-94%, which was better than the 50% expected by chance, and in accordance with our hypothesis. The correlation analysis using the Spearman's ρ test gave a statistically significant result of 0.35, interpreted as a moderately strong correlation between EQ-5D index change scores and PRWE-Swe change scores.

Table 1. *External responsiveness for EQ-5D index change scores for 132 patients with a surgically treated distal radius fracture.*

EQ-5D index score	**AUROC (95% CI)**	**Logistic Regression**	
		OR (95% CI)	**Correctly classified, %**
Clearly improved vs marginally/clearly deteriorated	0.75 (0.63-0.87)	1.06 (1.02-1.11)**	78
Marginally improved vs clearly deteriorated	0.70 (0.49-0.92)	1.05 (1.00-1.09)*	86
Marginally deteriorated vs clearly improved	0.71 (0.55-0.87)	1.05 (1.00-1.10)*	81
Clearly deteriorated vs marginally/clearly improved	0.76 (0.58-0.94)	1.06 (1.01-1.10)**	94

Note. Change scores in the PRWE-Swe between the 3- and 12-month follow-ups were used as EC. * $p<0.05$. ** $p<0.01$.
AUROC = area under receiver operating characteristic curve. CI = confidence interval. OR = odds ratio.

STUDY II

The results from this pragmatic RCT showed that the anesthesia method (RA or GA) did not influence the total opioid equivalent consumption (OEC) during the first 3 postoperative days (72 hours) following volar plate fixation of a DRF in adult patients treated in a day surgery setting. The two groups did, however, differ significantly with regard to the patterns of postoperative pain and opioid consumption within the first 24 hours of surgery; before discharge, patients in the GA group had significantly higher VAS for pain scores and OEC, while patients in the RA group had higher OEC after discharge on Day 1, as well as higher VAS for pain scores at 24 hours.

With regard to the postoperative pain peak (i.e. maximum postoperative pain during the first 24 hours), the intensity of pain as measured by VAS scores was similar between the two groups (GA: median, 7; width of IQR, 3; range, 0-10 and RA: median, 8; width of IQR, 2; range, 0-10), p=0.3), but the timing differed significantly; GA patients reported that the maximum pain occurred at a median of 1 hour (width of IQR, 8; range, 1-22) after the end of surgery, compared to 11 hours (width of IQR 7, range 1-24) among RA patients (p<0.001).

The median OEC for Days 1-3 for the RA and GA groups are presented in **Table 2**. There was no difference in duration of Day 1 in minutes between the two groups, taking into account the variability of the time of surgery (morning or afternoon).

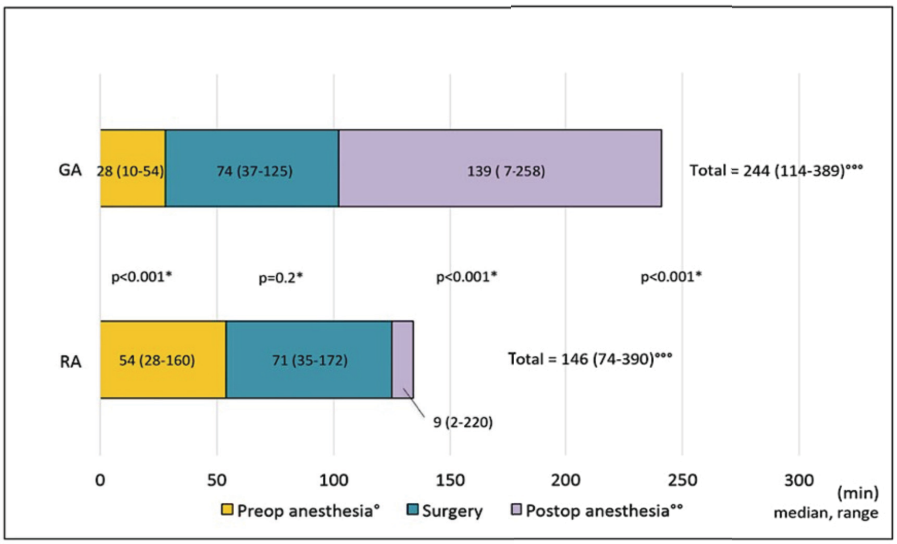
Table 2. *Median postoperative opioid equivalent consumption (OEC) in 88 adult patients undergoing volar plate fixation of a distal radius fracture in a day surgery setting and allocated to either regional anesthesia with a supraclavicular plexus blockade (RA) or general anesthesia (GA).*

	RA group (n=44)	**GA group (n=44)**	**p-value***
Day 1 total OEC[a] (mg)	23 (24, 0-75)	35 (45, 0-120)	0.005
Day 1 PO OEC before discharge (mg)	0 (6, 0-30)	0 (8, 0-68)	0.2
Day 1 IV OEC before discharge (mg)	0 (0, 0-30)	23 (26, 0-75)	<0.001
Day 1 PO + IV OEC before discharge (mg)	0 (6, 0-53)	26 (42, 0-104)	<0.001
Day 1 OEC after discharge (mg)	17 (18, 0-45)	11 (14, 0-45)	<0.001
Day 2 OEC[b] (mg)	23 (21, 0-59)	23 (32, 0-75)	0.4
Day 3 OEC[c] (mg),	15 (20, 0-60)	18 (26, 0-60)	0.3
Days 1-3 total[d] (mg)	60 (64, 3-150)	85 (96, 0-218)	0.1
Duration of Day 1[e] (min)	1020 (152, 765-1246)	1017 (265, 721-1250)	1.0

Note. Values are given as the median, with the width of the interquartile range (IQR), and the range. *Mann-Whitney U test. [a] From the end of surgery until 05:59 hours the following day, intravenous (IV) and peroral (PO). [b] From 06:00 hours on the first day after surgery until 05:59 the following day, PO. [c] From 06:00 hours on the second day after surgery until 05:59 hours the following day, PO. [d] From the end of surgery until 05:59 hours on the third day after surgery, IV and PO. [e]Time from end of surgery until 05:59 hours the following day, taking into account the variability of the time of surgery (morning or afternoon).

The total perioperative time consumption was longer for the GA group (median, 244 minutes; width of IQR, 65 minutes; range, 114-389 minutes) than for the RA group (median, 146 minutes; width of IQR, 57 minutes; range, 74-390 minutes) ($p<0.001$). Details of the surgical, preoperative, and postoperative anesthesia care time consumption for the two groups are presented in **Figure 4**.

After the first 24 postoperative hours, there were no significant differences between the RA and GA groups in any of the short- or longer-term outcomes, including range of motion, grip strength, EQ-5D-3L index score or PRWE-Swe score at 6 months.



*Mann-Whitney U test
°Preoperative anesthesia care time = from administration of plexus blockade for RA patients or induction of anesthesia for GA patients until "ready for surgery to start"
°°Postoperative anesthesia care time includes time in OR after the end of surgery for GA and RA patients, and time in the post anesthesia care unit (PACU) for GA patients, until discharge to the orthopedic ward
°°°Total perioperative time includes surgical duration, pre- and postoperative anesthesia care time

Figure 4. *Median perioperative time consumption (and range) in minutes for 88 patients undergoing volar plate fixation of a distal radius fracture in a day surgery setting and allocated to either regional anesthesia with a supraclavicular plexus blockade (RA) or general anesthesia (GA).*

STUDY III

The results from this national descriptive cross-sectional register study of 23,394 DRFs in 22,962 patients aged 18 years or older showed that a majority of all DRFs occurred in women (78%, n = 18,203/23,394), and that the mean age (± SD) was 65.4 ± 16.0 years for women, 53.6 ± 20.0 years for men and 62.7 ± 17.6 years for all. **Figure 5** visualizes the distribution of DRFs per age-interval and sex, and shows a steep rise in the number of DRFs in women 50 years or older.

The most common cause of injury was a simple fall (75%, n = 17,643/23,394). One third (33%, n = 7783/21,723) of all DRFs occurred at the patient's residence. The prevalence of DRFs was higher during the winter months (November through February), than the rest of the year.

Analysis of fracture classification data showed that 65% (n = 15,178/23,394) of all DRFs were classified as extra-articular AO-23-A, 12% (n = 2770/23,394) as partially intra-articular AO-23-B and 23% (n = 5446/23,394) as intra-articular AO-23-C. Only 1.2% (n = 289/23,394) of all DRFs were registered as open fractures. In **Table 3** detailed data on the distribution of all DRFs according to the AO/OTA classification in relation to patient-, fracture- and injury-related factors are presented.

The primary treatment was non-surgical for 74% (n = 17,358/23,369) and surgical for 26% (n = 6011/23,369) of all DRFs. Among AO-23-A fractures, only 18% received primary surgical treatment compared to 48% among AO-23-C fractures. Plate fixation was the most frequently used surgical method (82%, n = 4954/5972), followed by pin/wire fixation (8.2%, n = 490/5972), external fixation (4.8%, n = 289/5972) and other methods (4.0%, n = 239/5972). Among the DRFs treated non-surgically, 9.1% (n=1586/17,358) underwent secondary surgical treatment.

Among patients with a DRF, the overall 30-day mortality was 0.4% (n = 98/23,394) and the 1-year mortality was 2.9% (n = 679/23,394).

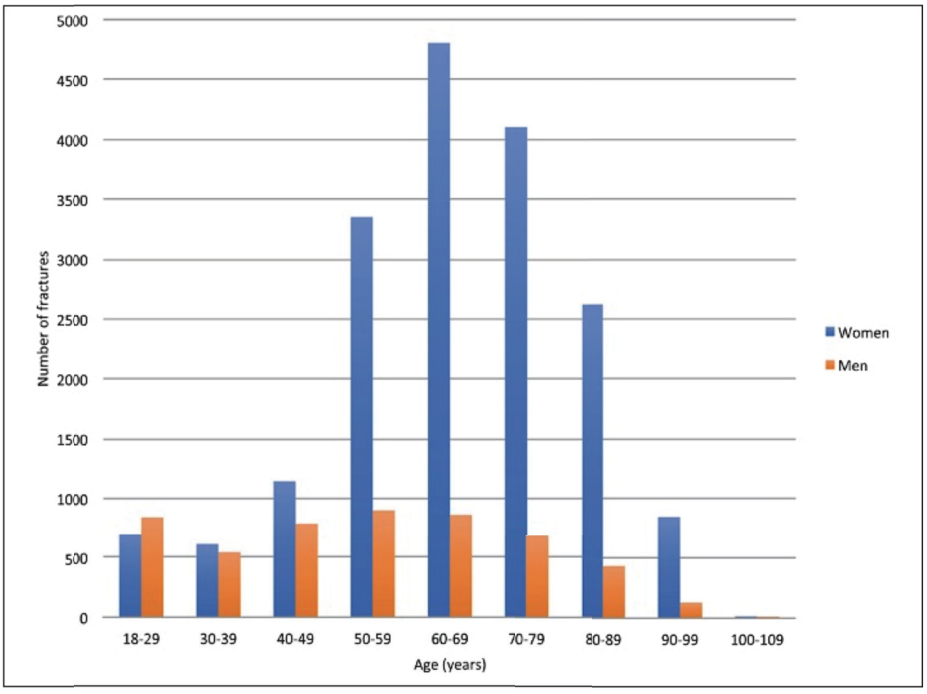


Figure 5. *Distribution per age-interval and sex of 23,394 distal radius fractures registered in the SFR during the years 2015-2017.*

Table 3. *Distribution per fracture type and group according to the AO/OTA classification system, in relation to age, sex, open/closed fracture and trauma mechanism (high/low-energy) of 23,394 distal radius fractures registered in the SFR during the years 2015-2017.*

Fracture type and group	Total n (%)	Mean ± SD age (years)	Women n (%)	Open fracture n (%)	High energy trauma n (%)
23-A2.1	5126 (22)	58.7 ± 18.7	3851 (75)	2 (0.0)	167 (3.3)
23-A2.2	7355 (31)	66.1 ± 16.9	6244 (85)	41 (0.6)	181 (2.5)
23-A2.3	529 (2.3)	64.3 ± 17.1	435 (82)	12 (2.3)	31 (5.9)
23-A3	2168 (9.3)	65.8 ±1 6.2	1838 (85)	80 (3.7)	94 (4.3)
Total 23-A	15,178 (65)	63.5 ± 17.8	12,368 (82)	135 (0.9)	473 (3.1)
23-B1	1377 (5.9)	56.0 ± 18.7	746 (54)	3 (0.2)	116 (8.4)
23-B2	638 (2.7)	61.8 ± 17.6	457 (72)	5 (0.8)	47 (7.4)
23-B3	755 (3.2)	61.3 ± 16.9	558 (74)	11 (1.5)	86 (11)
Total 23-B	2770 (12)	58.8 ± 18.2	1761 (64)	19 (0.7)	249 (9.0)
23-C1	2522 (11)	62.7 ± 16.4	1897 (75)	19 (0.8)	140 (5.6)
23-C2	1893 (8.1)	63.4 ± 16.4	1475 (78)	49 (2.6)	161 (8.5)
23-C3	1031 (4.4)	61.5 ± 16.6	702 (68)	67 (6.5)	179 (17)
Total 23-C	5446 (23)	62.7 ± 16.6	4074 (75)	135 (2.5)	480 (8.8)
All	23,394 (100)	62.7 ± 17.6	18,203 (78)	289 (1.2)	1202 (5.1)

STUDY IV

The results from this nation-wide cohort study of 31,807 patients aged 18 years or older with a surgically treated DRF, showed that the proportion of patients with a dispensed prescription of Flucloxacillin and/or Clindamycin within the first 8 weeks following surgery (i.e. a proxy for a surgical site infection) was 5% (n=1110/21,348) after plate fixation, 12% (n=754/6198) after pin fixation and 28% (n=1180/4261) after external fixation. The demographic characteristics of the study population is presented in **Table 4.**

Results of the logistic regression model are presented in **Table 5**. Surgery with external fixation displayed a strong association with the prescription of antibiotics (aOR 6.9, 95% CI 6.2-7.5, p<0.001), as did percutaneous pinning (aOR 2.7, 95% CI 2.4-3.0, p<0.001), compared to plate fixation (reference). Other factors associated with the prescription of antibiotics were open fracture type (aOR 6.4, 95% CI 5.3-7.6, p<0.001), and male sex (aOR 2.0, 95% CI 1.8-2.2, p<0.001).

The classification tree analysis showed that surgical method, fracture type (closed/open), sex and age were factors associated with the prescription of antibiotics. The highest proportion of antibiotics prescription was found among patients undergoing external fixation of an open fracture (58%), followed by externally fixated closed DRFs in men aged ≥ 75 years (53%).

Table 4. *Demographics of study population in Study IV; 31,807 adult patients undergoing surgical treatment of a distal radius fracture in Sweden between November 1st 2006 and October 31st 2013.*

Variable		Plate[a]	Pins[b]	EF[c]	All
		n (%)	n (%)	n (%)	n (%)
Age (years)	18-49	5016 (24%)	1197 (19%)	558 (13%)	6771 (21%)
	50-74	13,088 (61%)	3581 (58%)	2437 (57%)	19,106 (60%)
	≥75	3244 (15%)	1420 (23%)	1266 (30%)	5930 (19%)
Sex	Women	16,517 (77%)	5124 (83%)	3518 (83%)	25,159 (79%)
	Men	4831 (23%)	1074 (17%)	743 (17%)	6648 (21%)
Fracture type	Closed	20,969 (98%)	6131 (99%)	4072 (96%)	31,172 (98%)
	Open	379 (2%)	67 (1%)	189 (4%)	635 (2%)
Antibiotics[d] 0-8 weeks prior to DRF surgery	No	20,947 (98%)	6110 (99%)	4169 (98%)	31,226 (98%)
	Yes	401 (2%)	88 (1%)	92 (2%)	581 (2%)

[a] Plate fixation. [b] Percutaneous pinning. [c] External fixation. [d] A dispensed prescription of Flucloxacillin and/or Clindamycin.
n = numbers. DRF = distal radius fracture

Table 5. *Factors associated with a dispensed prescription of Flucloxacillin and/or Clindamycin within the first 8 weeks following distal radius fracture surgery in 31,807 adult Swedish patients. A logistic regression model was performed.*

Variable		Crude measures		Univariable		Multivariable, adjusted for all variables*	
		Total n	Antibiotics[d] 0-8 weeks after DRF surgery n (%)	OR	95% CI, p-value	OR	95% CI, p-value
Surgical method	Plate[a]	21,348	1110 (5%)	Ref.		Ref.	
	Pins[b]	6198	754 (12%)	2.5	2.3-2.8, <0.001	2.7	2.4-3.0, <0.001
	EF[c]	4261	1180 (28%)	7.0	6.4-7.6, <0.001	6.9	6.2-7.5, <0.001
Age (years)	18-49	6771	564 (8%)	Ref.		Ref.	
	50-74	19,106	1640 (9%)	1.0	0.9-1.1, 0.520	1.1	1.0-1.3, <0.038
	≥75	5930	840 (14%)	1.8	1.6-2.0, <0.001	1.6	1.4-1.8, <0.001
Sex	Women	25,159	2183 (9%)	Ref.		Ref.	
	Men	6648	861 (13%)	1.6	1.4-1.7, <0.001	2.0	1.8-2.2, <0.001
Fracture type	Closed	31,172	2776 (9%)	Ref.		Ref.	
	Open	635	268 (42%)	7.5	6.4-8.8, <0.001	6.4	5.3-7.6, <0.001
Antibiotics[d] 0-8 weeks prior to DRF surgery	No	31,226	2940 (9%)	Ref.		Ref.	
	Yes	581	104 (18%)	2.1	1.7-2.6, <0.001	1.6	1.3-2.1, <0.001

*Logistic regression model adjusted for surgical method, age, sex, fracture type (closed/open), and a dispensed prescription of antibiotics within 8 weeks prior to DRF surgery. [a] Plate fixation. [b] Percutaneous pinning. [c] External fixation. [d] A dispensed prescription of Flucloxacillin and/or Clindamycin. OR = odds ratio. CI = confidence interval. n = numbers. Ref. = Reference. DRF = distal radius fracture

DISCUSSION

Despite the facts that DRFs are the most common fractures treated in the health-care system, and that the existing literature is vast, consensus still lacks with regard to the optimal management of all subgroups of DRF patients, as well as on how treatment outcome is best evaluated. An evidence-based approach to the management of patients with a DRF requires a valid treatment algorithm capable of guiding clinical decision-making, taking into account fracture-, patient- and treatment-related factors including short- and long-term outcomes for each treatment method, as well as the spectrum and frequency of associated complications. Further, as public health resources are limited, the cost of treatments and their associated complications must also be taken into consideration.

The four studies included in this thesis have tried to fill some, however small, voids in the DRF literature by investigating aspects of epidemiology, surgical management and treatment outcome evaluation of DRFs in adults. A variety of study designs have been used, including: an assessment of the responsiveness of a widely used generic PROM (Study I), a pragmatic RCT (Study II), a descriptive cross-sectional study (Study III) and a cohort study (Study IV).

When interpreting results from any scientific study, one must be aware of the potential sources of error: random error and systematic errors (bias). The three main types of systematic errors include selection bias, information bias and confounding.[92] The four studies included in the thesis are discussed below with regard to main results, relation to previous research, as well as strengths and limitations, i.e. potential sources of error in study design and data sources.

EVALUATION OF OUTCOME AFTER DISTAL RADIUS FRACTURE TREATMENT

Study I was an assessment of the responsiveness (i.e. the ability to detect clinically relevant change over time) of the EQ-5D (specifically the EQ-5D-3L index score) in patients with a surgically treated DRF. The results showed an overall good internal and an acceptable to good external responsiveness of the EQ-5D index score in patients recovering from a surgically treated DRF.

The EQ-5D questionnaire is easily completed by the respondent and has a lower response burden than the also widely used SF-36,[61,62] thus reducing the risk of missing values. Given the generic design of EQ-5D, it enables comparisons of the impact on HRQoL between different treatments, diseases and injuries. Furthermore, it is often used in the calculation of QALYs in cost-effectiveness analyses.[84] However, with only 5 dimensions of health and 3 levels of response, it may not be responsive enough to adequately reflect change in the respondent's HRQoL for injuries and conditions with low morbidity. A previous review of 40 studies using EQ-5D to detect changes in HRQoL in a wide variety of patient groups confirmed that EQ-5D was more responsive when larger changes in health status was expected, such as after lower back surgery, high-dose chemotherapy for breast cancer and stroke rehabilitation.[93] Further, in a previous study assessing the responsiveness of SF-36, DASH and PRWE in patients recovering from a DRF,[86] PRWE displayed better responsiveness than DASH, which in turn was more responsive than SF-36. Thus, not

surprisingly, the more specific an instrument is for wrist disability, the more responsive it is in patients with a DRF. This was one of the reasons why PRWE-Swe was chosen over DASH as the external criterion (i.e. the gold standard to which EQ-5D was compared) in Study I, even though DASH was the primary outcome in the original RCT. Another reason was a lower response burden in PRWE compared to DASH.

The reason that the SRM was chosen over the also widely used standardized effect size (SES) as one of the measures of internal responsiveness, was that the SRM better reflects change over time than the SES. This since the SRM is determined by the mean change score divided by the standard deviation (SD) of the change score, as opposed to the SES, which is determined by the mean change score divided by the SD of the preinjury score.[94]

An important aspect of the interpretation of PROM results is the MID, i.e. the smallest difference in an instrument's score which reflects a relevant clinical change in patients. In the internal responsiveness analysis in Study I, the mean change score for the EQ-5D index score from preinjury state to the 3-month follow-up was statistically significant as well as clinically relevant, i.e. greater than the MID for the EQ-5D index score, while the mean change score between the 3- and the 12-month follow-ups was statistically significant but slightly smaller than the MID. Further, in the subgroup analysis of the external responsiveness of EQ-5D index score, only the mean change score of 12.1 in the clearly improved group was greater than the MID. This may indicate that EQ-5D is not responsive enough to detect the subtle changes in general HRQoL occurring between the 3- and the 12-month follow-ups in high-functioning individuals with a surgically treated DRF. This is in accordance with the results from previous studies in which EQ-5D proved more responsive for injuries and conditions associated with more morbidity.[93]

Further, the floor and ceiling effects should be considered in the analysis of PROM results. In Study I, the ceiling effect in the EQ-5D index score at baseline was 80%, which is high. It may reflect a high preinjury general HRQoL in the study population, but could partly be explained by an inadequate responsiveness of EQ-5D in patients with low morbidity, such as our study population.

A potential source of bias in Study I was the use of a value set from another country, as cultures may differ and affect how respondents value health states. In 2014, a Swedish value set was introduced,[84] however at the time when Study I was conducted, it had not yet been fully established, and we therefore used the well-known UK value set.[81,82]

Lastly, as only responsiveness was assessed in Study I, there is a lack of data on the reliability and validity of the EQ-5D index score in patients with a DRF. However, a recent literature review of the measurement properties of EQ-5D in patients with upper extremity orthopedic disorders concluded that EQ-5D displayed good reliability and validity in patients with upper extremity fractures or carpal tunnel syndrome.[95] As extrapolating results from other patient groups is not recommended, it would be reassuring to ascertain the reliability and validity of the EQ-5D index score in DRF patients in a future study.

ASPECTS OF ANESTHESIA IN DISTAL RADIUS FRACTURE SURGERY

Study II was a pragmatic RCT comparing general anesthesia (GA) and regional anesthesia with a supraclavicular plexus blockade (RA) in adult patients undergoing volar plate fixation of a DRF in a day surgery setting, with regard to early postoperative pain and opioid equivalent consumption (OEC), perioperative time consumption and longer-term functional outcomes and PROMs. The results showed that the anesthesia method significantly influenced the patterns of pain and OEC during the first 24 hours postoperatively, while neither total OEC during the first 3 postoperative days nor functional outcomes and PROMs at 6 months differed between the two groups. Further, the perioperative time consumption significantly differed between the GA and RA groups.

Our findings regarding early postoperative pain and OEC are in accordance with a previous smaller RCT by Galos et al, including 36 DRF patients followed for 3 months.[96] However, they reported a higher total mean OEC during the first 2 postoperative weeks in the GA group, but the clinical relevance of a mean difference of 5.4 mg over a period of two weeks could be questioned. Another RCT, by Hadzic et al,[97] showed similar results as ours with regard to early postoperative pain and analgesic intake over the first 48 hours for RA and GA groups, but contrary to our findings, they reported that RA patients had less pain and analgesic intake at 72 hours. However, as they included fewer patients, a variety of hand and wrist procedures were performed, the analgesics consumed after discharge were not specified and crossover cases from RA to GA were eliminated from the analysis, their results should be interpreted with caution. Further, in a similar RCT including 52 patients, published in 2020, Wong et al reported that DRF patients receiving RA with an infraclavicular nerve block had significantly lower pain scores than GA patients during the first 48 hours postoperatively.[98]

Our findings regarding the difference in patterns of early postoperative pain and OEC between GA and RA provide useful information for both DRF patients and treating surgeons. Patients may be guided in making an informed decision as to the choice of anesthetic method and how to tackle the pain of the early postoperative period, and surgeons in planning for and prescribing an adequate analgesic treatment. This conclusion is in line with Wong et al,[98] who reported a significant reduction of the rebound pain (i.e. postoperative pain peak experienced by RA patients as the effect of the nerve block ceases), by prescribing patients a regular postoperative scheme of acetaminophen, starting at return to the ward, in combination with patient education. However, based on our results, we believe that a multimodal analgesic approach including opioids in addition to acetaminophen, is necessary for adequate pain relief during the first postoperative days for most patients undergoing plate fixation of a DRF.

The analysis of the perioperative time consumption in Study II showed that the total perioperative time was significantly longer in the GA group compared to the RA group, and that this was primarily caused by a significantly longer time in the PACU for GA patients. Surgical suite time did not differ between groups. Our findings are in accordance with those of Galos et al.[96] These results may guide hospitals in the planning and allocation of anesthesia resources and personnel for this common patient group. Furthermore, we found that, although not statistically significant, the rate of unplanned admissions was 16% in the GA group and 5% in the RA group. Our findings of a longer perioperative time consumption and the trend towards more unplanned admissions among GA patients suggests that this anesthesia method

may be associated with a greater consumption of health-care resources in DRF surgery, although further studies are needed to verify this.

Regarding the longer-term outcomes, we can conclude that the anesthesia method did not influence the function, patient-reported general HRQoL or patient-reported wrist function and pain at 6 months. Our findings are in accordance with those of Galos et al,[96] and Wong et al,[98] as well as our clinical experience, but they are contrary to the results from a previous non-randomized retrospective study by Egol et al,[99] who reported better functional outcome and DASH scores for RA patients at 3 and 6 months after DRF surgery.

A major strength of Study II was its randomized design, minimizing the risk of confounding. The single-center design, prospective follow-up and the low loss to follow-up reduced the risk of selection and information bias. The generalizability of the results was warranted by a combination of good precision, high internal validity and a pragmatic study design.

The OEC was chosen as the primary outcome in Study II because we considered it to be a more objective variable than the subjective VAS for pain. We expected any possible differences in opioid metabolism between patients to be neutralized by randomization. However, the study patients' attitudes toward opioid consumption as well as the treating surgeons' opinions may have influenced the OEC.

The decision to only report on the consumption of opioids in Study II, was supported by results from a previous study,[100] in which the consumption of over-the-counter analgesics, including NSAIDs and acetaminophen, did not influence the mean OEC after open DRF surgery in patients receiving either GA or RA.

Lastly, variations in procedural routines of regional anesthesia between different hospitals and countries, may affect the generalizability of the results.

EPIDEMIOLOGY OF DISTAL RADIUS FRACTURES IN ADULTS

Study III was a national descriptive cross-sectional register study of the epidemiology, classification, treatment and mortality of DRF in adults, using data from the Swedish Fracture Register (SFR) for the years 2015-2017. It provided comprehensive epidemiological data on 23,394 DRF in 22,962 patients aged 18 years or older.

The main finding of Study III was that the majority of DRFs occurred in women 50 years or older, as a result of a low-energy simple fall, often at the patients' own residence.

The majority (78%) of all DRFs occurred in women, which is in accordance with the results from a previous Swedish regional study, reporting the same proportion,[101] while it is slightly higher than the proportion of women of 75% reported in a population-based Swedish register study,[2] and much higher than the 68% reported in a British regional study.[5] Furthermore, there was a great increase in the number of fractures in women aged 50 years or older, compared to younger women, as well as all adult men. These findings are in line with previous studies,[1-5] and are interpreted as an expression of the well-known association of decreased bone mineral density in postmenopausal women and DRFs.[12-14]

Study III provided unprecedented data on the distribution of DRFs in the adult Swedish population according to the AO/OTA fracture classification system, in relation to patient-, fracture- and trauma-related factors. While a majority (65%) of all DRFs were extra-articular (AO-23-A), only 12% were partial articular (AO-23-B), and 23% complete intra-articular (AO-23-C). For AO-23-B and AO-23-C fractures, the proportion of men was higher, the mean age slightly lower, and a high-energy trauma mechanism was more common than for AO-23-A fractures. The proportion of all DRFs classified as an open fracture was only 1.2%, which is in line with the results (0.8%) from a previous regional Swedish register study.[34] Of note is that among AO-23-C3 fractures, the highest proportion of both open fractures (6.5%) and high-energy trauma mechanism (17%) was found.

With regard to primary treatment, we found that 26% of all DRFs in adults were treated surgically in Sweden during 2015-2017. This is considerably higher than the results from a previous population-based cohort study, which reported a proportion of surgically treated DRFs in Swedish adults of 16% in 2005 and 20% in 2010.[2] Our results may suggest a continued tendency to treat more DRFs surgically, however, due to the possibility that non-surgically treated DRFs are underreported in the SFR, this result should be interpreted with caution. Interestingly, only 18% of AO-23-A fractures were treated surgically compared to 48% of AO-23-C fractures. We speculate that this is explained by an increased inherent instability and risk of joint surface displacement in AO-23-C fractures, in combination with a higher proportion of open fractures and high-energy trauma mechanism. Furthermore, we found that the most frequently used surgical method in primary surgical treatment was plate fixation (82%), followed by pin fixation (8.2%), external fixation (4.8%) and lastly other methods (4.0%). This is line with previous studies reporting that plate fixation has become the method of choice in recent decades.[2,4,33-38]

Our finding of a seasonal variation in the occurrence of DRFs, with an increased number of DRFs during the winter months (November through February), is in line with previous studies.[5-8,102,103] An association to more slippery walking conditions due to ice and snow in the winter months has been suggested,[6,8] but seasonality has been reported from countries and regions with mild winter climate as well, indicating that other factors also play a part.[102,103]

The major strength of Study III was the great number of included fractures. Secondly, the SFR provides prospectively registered data from most parts of Sweden, thus reducing the risk of bias due to sociodemographic regional differences and varying local treatment traditions. Thirdly, the study period encompassed 3 years, recent in time, which reduces the risk of influence on fracture prevalence from extreme variations in weather conditions in a specific year, as well as warrants relevance of the results to current practice.

The most obvious limitation of Study III was the lack of full national coverage of the SFR, even though it improved during the study period so that by the end of 2017, the proportion of affiliated departments was more than 80% of all Orthopedic departments in Sweden. The incomplete national coverage made calculation of incidence rates impossible. Another limitation was that non-surgically treated DRFs may be underreported in the SFR, as a proportion of DRFs not in need of either reduction nor surgery are likely treated by primary care units, not affiliated to the SFR. Further, the lack of validation of the fracture classification of DRFs in the SFR may have been a limitation.

Finally, as this was a descriptive study, causality could not be assessed. However, the results paint a detailed and up-to-date picture of the DRF epidemiology and current practice in the Swedish adult population, and may be useful in generating hypotheses for future studies.

SURGICAL SITE INFECTION AFTER DISTAL RADIUS FRACTURE SURGERY

Study IV was a national cohort study assessing the rate of surgical site infection (SSI) after DRF surgery, as well as factors associated with an SSI. Data was linked from two national population-based health-care registers, the NPR and the SPDR, and a dispensed prescription of Flucloxacillin and/or Clindamycin within the first 8 weeks following surgery was used as a proxy for an SSI. A total of 31,807 patients with a surgically treated DRF were included.

The main findings were that the rates of SSI were 28% after external fixation, 12% after percutaneous pinning and 5% after plate fixation. Previous literature on the rate of SSI after DRF surgery mainly comprise RCTs comparing surgical methods for DRFs with regard to functional outcome and PROMs, reporting SSI as a secondary outcome. The rates of SSIs presented in these studies range from 0-5.6% after plate fixation,[27,29-31,45,104] 7.8-23% after percutaneous pinning,[29,30,45] and 5.3-26% after external fixation.[27,31,45,104] Further, a few previous meta-analyses and systematic reviews have synthesized the data from the mentioned RCTs, as well as from existing retrospective case series, presenting the following rates of SSI: 7.7% (range 0-15%) after percutaneous pinning,[105] 3.2% after volar plate fixation compared to 8.2% after percutaneous pinning,[106] and 0.5% after volar plate fixation compared to 7.7% after external fixation.[107]

Our results showed that factors associated with an SSI were surgical method, fracture type (open/closed), sex and age. In the classification tree analysis, the highest proportion of antibiotics prescription was found among patients treated with external fixation for an open fracture (58%), followed by externally fixated closed DRFs in men aged 75 years or older (53%). These findings may be useful for physicians when evaluating the risk for SSI after DRF surgery for individual patients. While open fracture type is a well-known and uncontradicted risk factor for SSI,[48] the previous literature on other associated factors is scarce. In a previous retrospective study of risk factors for pin site infection in 1213 patients treated with percutaneous pinning in the wrist and/or hand, no individual factor was found to be associated with pin site infection in their multivariable analysis.[108] Our results showed an association between male sex and antibiotics prescription, as indicated by adjusted OR of 2.0 in the multivariable logistic regression model, and a higher proportion of antibiotics prescription compared to women regardless of surgical method and node level in the classification tree analysis. We speculate that this may be due to a higher proportion of high energetic trauma in men with a subsequent increased risk of SSI, or a tendency among physicians to prescribe antibiotics in a greater extent to men than women. However, further studies are needed to investigate this.

A major strength of Study IV was the great number of included patients in the analysis, warranting high precision. Further, the coverage of the population-based registers used, the NPR and the SPDR is high, reducing the risk of both selection bias and loss to follow-up. Further, as patients from all regions in Sweden were included, and the study period included seven years, the influence from regional differences in treatment tradition is minimized, as

well as influence from annual and seasonal changes in incidence. The study period covered the years 2006 to 2013. While treatment trends of DRFs have changed since the study ended, with a continued increase in popularity of volar plate fixation and a concomitant decrease in external fixation, we believe that by investigating a period during which external fixation was still a part of the standard treatment arsenal for displaced DRFs, we provide valuable comparative data.

Limitations of Study IV included the fact that the NPR lacks detailed patient- and fracture-related data relevant to fracture treatment, including comorbidities, smoking, fracture side and fracture classification. Further, the NCSP-S code for plate fixation in the NPR does not differentiate between volar, dorsal or multiple plating. While a volar approach is gold standard, dorsal and multiple approaches are rare and mainly used for a subset of complex DRFs. As complex fractures are likely to have an increased risk of SSI, this may introduce bias. It would have been preferable to exclude dorsal or multiple plating from the plate group in order to gain a clearer understanding of the infection burden after a standard volar plating procedure. In addition, the NPR coding for percutaneous pinning does not provide information on whether the pins were buried under the skin or not. However, a recent Cochrane review of percutaneous pinning in the treatment of DRFs found only low-quality evidence that the burying of pins reduces the incidence of superficial infections.[105] The total number of fractures in our analysis may be slightly underestimated since patients with concomitant bilateral DRFs or a recurring DRF within the study period were only accounted for once. However, we do not believe that this affects the three exposure groups differently. Lastly, the lack of validation of DRF codes in the NPR is a limitation.

The time period after surgery during which the SPDR was screened for a dispensed prescription of Flucloxacillin and/or Clindamycin was set to 8 weeks based on our clinical experience as well as previous research.[48,49,52] In doing so, late onset surgical site infections occurring after 8 weeks were missed, but based on our clinical experience we believe that these are rare in DRF surgery.

We chose to use a proxy for an SSI since the coding for SSI in the NPR is not reliable. Further, given the strongly regulated pharmaceutical system in Sweden and the Swedish strategic program against antibiotic resistance (STRAMA),[109] which guides antibiotics use in Sweden, we believe that the use of a dispensed prescription of peroral Flucloxacillin and/or Clindamycin as a proxy is valid. We are aware that, as the SPDR provides information on dispensed prescription drugs only, this may be a reason for underestimation of the primary outcome in our study. Likewise, an overestimation of the outcome may be present due to prophylactic prescription of antibiotics for postoperative swelling and pain without positive bacterial culture findings, as well as prescription due to other reasons than an SSI.

CONCLUSIONS AND CLINICAL IMPLICATIONS

STUDY I

EQ-5D index score displayed an overall acceptable to good responsiveness in adults with a surgically treated DRF, and may thus be used as a patient-reported outcome measure of HRQoL in DRF patients. This further enables comparisons of HRQoL with other patient groups, as well as calculations of QALYs in cost-effectiveness analyses.

STUDY II

The anesthesia method (regional or general) significantly influenced the pattern of postoperative pain and opioid consumption over the first 24 hours after day surgery with volar plate fixation of a DRF in adults, as well as the perioperative time consumption. However, neither the total opioid equivalent consumption (OEC) over the first 3 postoperative days nor longer-term functional and patient-reported outcomes differed between the two groups. The results may be an aid in deciding on the type of anesthesia for adult patients undergoing surgery of a DRF, not least by helping patients making an informed decision and be better prepared for the early postoperative period with regard to expected pain and analgesic need. They may also guide the treating surgeon in planning for an adequate postoperative analgesic treatment and highlights the importance of informing day surgery patients receiving regional anesthesia about the intense pain that may occur after discharge when the effect of the nerve block ceases, and how patients should prepare for this by the intake of adjuvant analgesics. Lastly, the results regarding perioperative time consumption may guide hospitals in planning for anesthesia resource and personnel allocation for this common patient group.

STUDY III

The most common type of patient was a woman 50 years or older, who sustained a DRF through a simple fall at her own residence, and whose fracture was extra-articular and treated non-surgically. This descriptive national register study provided up-to-date comprehensive data on the epidemiology, fracture classification, injury characteristics, treatment regimens and mortality of DRFs in the adult Swedish population.

STUDY IV

The rate of surgical site infection (SSI) was highest after external fixation and lowest after plate fixation. Factors associated with an SSI were surgical method, fracture type (open/closed), sex and age. The results may be used for estimation of the postoperative infection burden after DRF surgery on a population basis. For the treating physician, they may aid in estimating the risk of SSI for individual patients.

FUTURE PERSPECTIVES

During the course of this doctoral project, the following ideas for future studies have emerged:

- There is still debate as to which treatment method is superior in several subgroups of DRF patients. In order to reach consensus and provide a more evidence-based practice for all patients with a DRF, there is great need for well-designed well-powered multi-center randomized clinical trials comparing the main treatment methods with regard to longer-term PROMs, as well as functional and radiographic outcomes. Maybe a way to do this could be a register-based RCT, using the SFR.

- There is need for a classification system of DRFs which takes into account radiologic appearance as well as fracture-, injury- and patient-related factors, with the purpose of providing prognostic information and a valid treatment algorithm for patients with a DRF. Cost of treatment and potential complications in relation to expected treatment outcome should also be considered in the algorithm.

- When evaluating treatment outcome with PROMs, instruments should have high validity, reliability and responsiveness for the intended patient group. There is great need for a new and even more responsive PROM for patients recovering from a DRF, which takes into account patient-related factors such as handedness, age and activity level, and includes questions on wrist pain and disability in situations relevant to modern life, such as using a smart phone or computer.

- Although the proportion of surgically treated DRFs has increased over recent decades, the vast majority of all DRFs are still treated non-surgically. Future studies are needed to assess the optimal length of immobilization for non-surgically treated DRFs with regard to short- and long-term functional outcome, PROMs and radiographic appearance, for all subgroups of DRF patients, as well as the optimal timing of follow-ups with regard to potential loss of fracture reduction.

- Lastly, the literature on DRF epidemiology and treatment is extensive, heterogenic and of varying quality. It is difficult to get an overview of the field. Current practice may, thus, not always be based on evidence, but rather on current trends, influence from implant industry and surgeons' preferences. The need for up-to-date meta-analyses and systematic reviews synthesizing current evidence is great.

POPULÄRVETENSKAPLIG SAMMANFATTNING PÅ SVENSKA

En distal radiusfraktur kallas i vardagligt tal för handledsfraktur och innebär ett benbrott i strålbenets nedre del, där detta övergår i en led mot handlovsbenen. Det är den allra vanligaste frakturtypen. Handledsfrakturer kan skilja sig åt från en enkel spricka utan felställning till en komplicerad instabil fraktur med många lösa benbitar, en stor felställning av ledytan samt öppna sår. Därför varierar även behandlingen från elastisk linda till omfattande öppen kirurgi. Cirka fyra av fem handledsfrakturer behandlas icke-kirurgiskt, oftast med gipsskena. För de handledsfrakturer som opereras, utgörs den vanligaste metoden av öppnande av huden, tillrättaläggande av lösa benbitar och fixering med platta och skruvar (plattfixation). Andra vanliga metoder innefattar; extern fixation, då frakturen manipuleras från utsidan varefter läget låses med en yttre metallställning; samt perkutan stiftning, då frakturläget efter yttre manipulation låses med metallstift som förs in i strålbenet genom små öppningar i huden. Metallställning och stift tas bort efter läkningstiden på 4-6 veckor. Kirurgi av handledsfrakturer sker oftast i dagkirurgi, dvs patienten kan gå hem samma dag. Bedövning under operationen åstadkoms antingen genom sövning eller genom blockad av enbart den skadade armen. En välkänd komplikation vid kirurgi är infektion i operationsområdet. Besvär som kan kvarstå länge efter behandling av en handledsfraktur innefattar smärta, stelhet, nedsatt greppstyrka samt nedsatt allmän hälso-relaterad livskvalitet. Ett viktigt mått på utfall av behandling är patient-rapporterad hälsa, livskvalitet och funktion.

Avhandlingens övergripande syfte var att bidra till en förbättrad behandling av patienter med handledsfraktur. De fyra delstudiernas respektive syfte och resultat var följande:

Studie I undersökte om den ofta använda enkäten för patient-rapporterad allmän hälsorelaterad livskvalitet, EQ-5D, hade tillräckligt god förmåga att fånga upp förändringar i hälsorelaterad livskvalitet (s k responsivitet) hos 132 patienter som återhämtade sig efter operation av en handledsfraktur. Studien visade att EQ-5D är tillräckligt ”responsiv”.

Studie II jämförde bedövningsmetoderna sövning respektive nervblockad av armen hos 88 patienter med en handledsfraktur som opererades med plattfixation i dagkirurgi. Smärta och intag av morfinpreparat under de tre första dagarna efter operationen, samt handledsfunktion och patient-rapporterad hälsa och funktion efter 6 månader jämfördes mellan grupperna. Studien visade att bedövningsmetoderna skiljde sig åt avseende mönster av smärta och intag av morfinpreparat under det första dygnet efter operationen, men därefter observerades inga skillnader.

Studie III var en beskrivande nationell registerstudie för att kartlägga förekomst och karakteristika för handledsfrakturer hos vuxna. I studien presenteras detaljerade patient-, fraktur-, skade- och behandlingsrelaterade data för 23 394 handledsfrakturer hos 22 962 patienter.

Studie IV var en befolkningsbaserad nationell registerstudie som jämförde förekomsten av infektioner i operationsområdet för de tre vanligaste kirurgiska metoderna som används för handledsfrakturer hos vuxna. Studien visade att infektioner i operationsområdet var vanligast efter extern fixation och minst vanligt efter plattfixation.

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